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HL

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/306,006	05/06/99	SUPERSAXO A	NB/2-21551/A

000324 HM22/1207
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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1616	4

DATE MAILED: 12/07/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/306,006	Supersaxo et al
Examiner	**Group Art Unit**
Shahnam Sharareh	1616

☒ Responsive to communication(s) filed on *May 6, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-27* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-27* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2,3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-27 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (I) a composition comprising a membrane forming, a coemulsifier and a lipophilic component, and (II) methods of preparing said composition by steps comprising mixing, stirring or heating said components, does not reasonably provide enablement for methods of preparing said compositions without employing any additional supply of energy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention without undue experimentation.

In particular, the specifications fails to enable the skilled artisan to practice the invention without undue experimentation. As held by *ex parte Forman* (230 USPQ 546, BdPatApp & Int.) and *In re Wands* (858 F.2d 731, 8 USPQ2d 1400, 1404, Fed. Cir. 1988) provide several

guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation.

The state of the prior art concerning methods of making microemulsion employs to methods that utilize an energy source such as a heating device, or stirring mechanism. However, the specification of instant application of preparing a nanodispersion without an external energy source does not describe the mechanism neither the dynamics of such preparation process. Further, the specification; specifically the examples (pages 10-15), disclose methods of preparing the instant compositions using various sources of external energy. In addition, there is not prior knowledge whether the claimed composition can be prepared in the manner that no external energy supply is used to form a transparent homogenous preparation from heterogeneous components, in fact such claim is in contrary to the basic thermodynamic laws. Therefore, there is no predictability in the art concerning such methods of preparing a pharmceutical formulation. Thus, the amount of guidance presented in the specification fails to present a required amount of guidance to perform the claimed method without undue experimentation.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 1-27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what does the applicant means by reciting the limitation "steps (α) and

(β) being carried out without any additional supply of energy." This statement is in contrary to basic thermodynamic laws.

5. Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claim is vague because it is not clear what is meant by recitation of "using a nanodispersion." in preamble. In the instant claim, it is not clear how is the nanodispersion used in preparing a pharmaceutical formulation. The instant method is missing the essential step of using a nanodispersion in the process.

6. Regarding claim 1, the phrase "so called nanodispersion prephase" renders the claim indefinite because it is unclear whether this limitation(s) is part of the claimed invention. See MPEP § 2173.05(d).

7. Claim 5 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Recitation of the phrase "preferably form o/w" renders the claim vague, because it is not clear what type of substances is the applicant reffering to as the claimed invention.

8. Claims 16-18 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are confusing because it is not clear what is meant by "pharmaceutical end formulation."

9. Claim 22-23 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation of "per se" renders the claim vague and confusing.

10. Claim 1, 27 recites the limitation "the water phase of the pharmaceutical end". There is insufficient antecedent basis for this limitation in the claim. Claim does not recite the presence of any water phase or any pharmaceutical end in the instant method.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-3, 5-13, 15-17, 20-21, 25-27 rejected under 35 U.S.C. 102(b) as being anticipated by 5,171,566.

The instant claims are directed to methods of preparing a composition comprising mixing a membrane forming molecule, a coemulsifer and a lipophilic component with a pharmaceutical agent. The instant claims are also directed to nanodispersion compositions comprising a membrane-forming molecule, coemulsifier, and a lipophilic component.

Mizushima et al disclose an ophthalmic preparation which can be prepared in the form of a fat emulsion comprising soybean oil (lipophilic component), a phospholipid (a membrane forming molecule), and various stabilizers such as polyoxyethylene-polyoxypropylne copolymers, and

active agent such as flurbiprofen (see col 3 lines 1-35, examples 1-3) Mizushima et al also disclose methods of mixing the components of said preparation, and further heating the mixture to obtain an oil-in-water emulsion (see col 3 lines 24-35.) Mizushima et al further disclose that their preparation can also be made in the form of an ointment or a lotion (see col 3 lines 39-41.) Therefore, Mizushima meets the limitations set forth in the instant claims.

13. Claims 25-27 rejected under 35 U.S.C. 102(b) as being anticipated by Nakajima et al US Patent 5,338,761.

The instant claims are also directed to nanodispersion compositions comprising a membrane-forming molecule, coemulsifier, and a lipophilic component.

Nakajima et al disclose an emulsified composition having an average particle size of 0.01 to 0.070 μm comprising a lipid soluble portion which may comprise a pharmaceutical agent, a phospholipid (a membrane forming molecule), and water, wherein the lipid soluble portion is preferably 1%-40% by weight (see abstract and col 4 lines 10-16.) Nakajima et al also disclose various types of surfactant such as polyoxyethylene derivatives, and various types of phospholipids that may be used in making their composition (see col 3 lines 1-34.) Therefore, Nakajima et al meet the limitations set forth in the instant claims.

Claim Rejections - 35 USC § 102/103

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 1-27 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Owen et al US Patent 5,633,226.

The instant claims are directed to methods of preparing a pharmaceutical composition comprising mixing a membrane forming molecule, a coemulsifer and a lipophilic component with a pharmaceutically active agent. The instant claims are also directed to nanodispersion compositions comprising a membrane-forming molecule, coemulsifier, and a lipophilic component.

Owen et al disclose W/O microemulsions which converts to an oil in water emulsion when added to an aqueous fluid (see abstract.) The biologically active composition of Owen et al comprise oil dispersible surfactant comprising a membrane forming material such as phospholipids (see col 7 lines 19-29.) in mixture with other surfactant, a pharmaceutically acceptable oil, an aqueous phase, and a water-soluble bioactive agent (see col 4 lines 49-60.)
Owen et al also disclose the preferred weight percentages of the individual components of their emulsion (see col 5 lines 12-55.), various non-ionic surfactant (coemulsifiers) such as

polyoxyethylene derivatives (see col 7 lines 31-54.) in various dosage formulations of their composition such as creams, suppositories or oral capsules (see col 6 lines 6-35, col 15 lines 20-27.) Owen et al further teach that the water component of the aqueous phase can be partially or fully replaced by other polar solvents such as poly hydrolic alcohols, or propylene glycol, thus allowing the components to be mixed in an anhydrous medium formulating a dehydrated preparation (see col 5 lines 44-50.) Finally, Owen et al teach methods of preparing their composition comprising mixing the individual components, and adding the pharmaceutical agent to the water phase of the prepared mixture in the manner that no high-energy mixing or application of heat is required (see col 10 lines 56-67, col 11 lines 1-10, col 15 lines 59-67, and col 16 lines 1-21.)

Accordingly, Owens et al anticipates the limitations set forth in the instant claims. However, the instant claims additionally describe the process of preparing a pharmaceutical composition to comprise a mixing step that is carried out without an energy supply. In such case, it would have been obvious to one ordinary skilled in the art at the time of invention to utilize the teachings of Owens et al and select pharmaceutical active agents described in the art that can be soluble in both water-in-oil or oil-in-water emulsions and further formulate emulsions that are prepared at room temperature without employing high-energy mixing.

Conclusion

No claims were allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose

telephone number is (703) 306-5400. The examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Jose Dees can be reached on 703-308-4628. The fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.

sjs, 12/2/99

SHELLEY A. DODSON
PRIMARY EXAMINER